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THE DESIGN AND CONSTRUCTION OF A THERMAL SYSTEM TO MEASURE SMALL TEMPERATURE CHANGES IN THE BRAIN

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Abstract

A system is described by which small localized temperature changes can be measured in the brain. The system includes 3 types of probes, a thermistor-electrode probe, heated-thermistor probe and a differential-thermistor probe. An a.c. compensating ratio bridge when used with a low noise/high gain amplifier linearizes the response of the thermistor over the temperature range used. It is possible to detect temperature changes as small as .0002°C with this system.

1. INTRODUCTION

One of the unique properties of the brain is that it is made up of discrete structures of nerve cells that regulate different functions of the organism. Recent experimentation has shown that it is possible to measure small localized temperature changes in these structures (1, 2). Temperature increases as well as decreases of the order .001°C to .01°C can be detected in various parts of the visual, auditory and somatosensory systems of the brain. These thermal changes are dependent upon the sensory stimulation used and can be correlated with electrical as well as the metabolic activity of the individual regions of the nervous system.

Temperature change in the brain is not a monomial phenomenon. There are several factors that can bring about thermal changes either locally or throughout the entire brain. First, neural metabolic heat (NMH) is produced by the firing of a nerve cell and the concomitant biochemical processes that accompany it. Second, as the blood is generally cooler than the brain, temperature change is brought about by adjustment or alteration of the rate of blood flow. As nerve cells fire, they demand more oxygen and glucose and so there is a call for an increased blood supply. Besides being highly vascularized, the brain has a heterogeneous distribution of capillary vessels. Blood flow rates and capillary density vary from one structure to the other. Therefore, this effect varies from one part of the brain to the other. Thirdly, even if the blood flow rate remains constant, temperature changes can take place in other parts of the body through the physical activity of muscle groups or metabolic functioning of other organs. Such a change would be transmitted by the common blood supply and would be reflected throughout the entire brain.

Most of the energy that the brain utilizes to produce electrical impulses in the neurons or nerve cells is derived from the oxidation of glucose. Such a reaction produces 5 calories for every milliliter of oxygen used. The brain consumes approximately 1/5 of the body's supply of oxygen but makes up only about 1/50 of the entire body weight. On the basis of these glucose oxidation measures and total brain blood supply, it has been estimated that the heat output of the brain is 4.8 cal/sec or 20 watts of power. For small discrete cellular regions of the brain, estimates of 6500 μcal/g/sec have been made (2).

Considering the fact that these thermal changes are small and that the range in temperatures normally encountered in the mammal (for our experiments, the cat) does not vary more than ± 3°C, it was necessary to design a system that would be extremely sensitive over a relatively small temperature range.

2. DESIGN OF THE THERMAL SYSTEM

2.1 THREE TYPES OF THERMAL PROBES

There are several considerations in the design of thermal probes for measurement of brain temperature. It is necessary that the probe have a high sensitivity in order to monitor the small temperature changes that take place in the brain. Relatively small size and use of non-toxic substances are essential in order to keep tissue damage to a minimum. Ease of construction and thermal insulation are also important factors.

2.1.1 Thermistor-Electrode Probe

The probe depicted in Figure 1A is used to measure brain temperature via an ultra small thermistor bead (VECO 41A14 10 kΩ @ 25°C). The platinum electrodes monitor the concomitant electrical activity of the area under investigation. In addition, with proper biasing and reference electrodes the platinum wires can measure oxygen availability. This probe is easily constructed from a four hole alumina ceramic-type rod (Omega Engineering Co.). The short leads of the thermistor are microwelded to 2 wires (.001" dia) and threaded through 2 holes of the rod. The platinum wire electrodes are threaded through the remaining 2 holes. A drop of Epoxylite varnish is deposited on the end of the probe to insure electrical insulation. After the varnish cures, the thermistor is calibrated and the probe is implanted in the brain. It is fixed to the skull by means of screws and dental cement. The wires are soldered onto a connector plug that is also attached to the skull with dental cement. Figure 2 is an example of temperature changes that have been recorded with similar probes. These previously reported results (2) are examples of simultaneous recordings in 2 different structures in the brain.

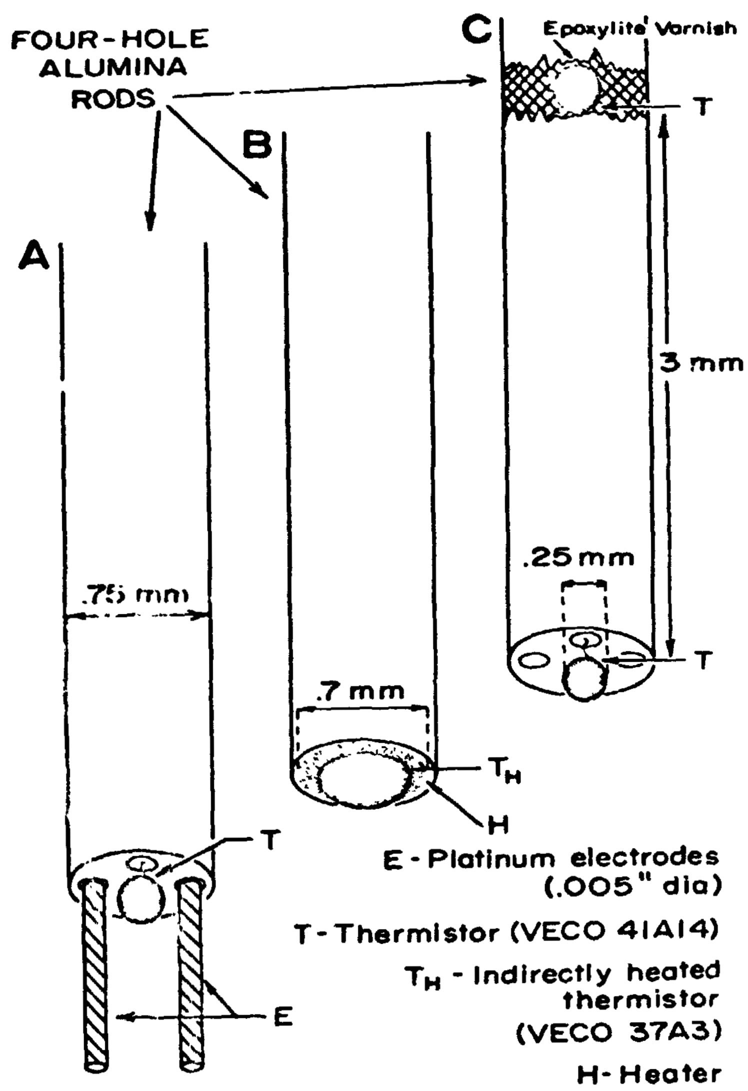


Figure 1. Three types of thermal probes used to measure temperature in the brain. (A) thermistor-electrode (B) heated-thermistor and (C) differential-thermistor.

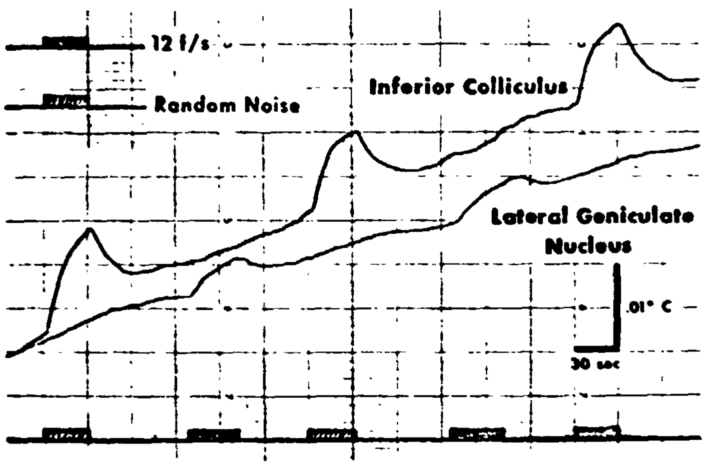


Figure 2. Simultaneous recording of localized thermal responses evoked in the inferior colliculus by stimulation of the ear with random noise and in the lateral geniculate nucleus by stimulation of the eye with light flashes (12 flashes/sec). Time markers indicate stimulation periods (2).

2.1.2 Heated-Thermistor Probe

A probe to detect temperature changes caused by cerebral blood flow alterations is depicted in Figure 1B. It is constructed in a manner similar to that of the thermistor-electrode probe but the ultra small bead has been replaced with an indirectly heated thermistor (VECO 37A3 7 KΩ @ 25°C). Two of the wire leads are connected to the low resistance (20 Ω) semi-conductor heater and the other two are attached to the thermistor. By applying a current to the heater, the temperature of the thermistor is raised above that of the surrounding brain tissue. Therefore, temperature changes that are due to alteration in the rate of blood flow can be separated from those produced by neural metabolic heat. Such a technique has been used for many years to detect blood flow changes in many parts of the body (3, 4). Figure 3 is an example of the temperature changes recorded when an indirectly heated thermistor probe is used.

2.1.3 Differential-Thermistor Probe

Finally, a probe to record differential thermal activity is presented in Figure 1C. The

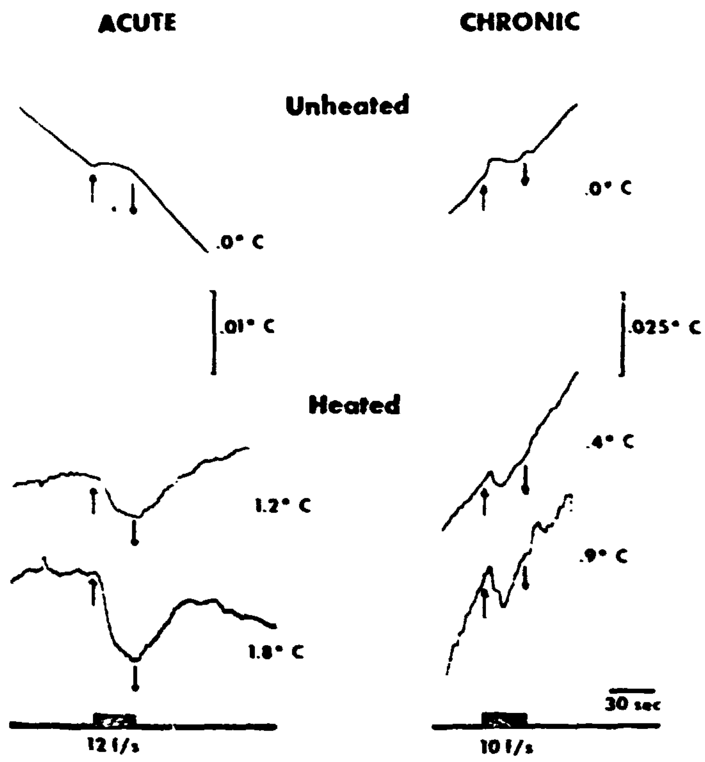


Figure 3. Thermal responses evoked in the lateral geniculate nucleus by stimulation of the eye with flashing light (12/or 10/ sec). These responses were obtained before (top) and after (bottom) the thermistor is heated above that of the surrounding tissue by 0.4-1.8°C. Reversal of thermal response indicates that a change in blood flow takes place. Left: responses from an acute or anesthetized cat. Right: responses from a chronic or awake animal. Time markers and arrows indicate stimulation periods (2).

small localized temperature changes described above are superimposed on a constantly varying temperature baseline that is present throughout the entire brain. Often these generalized temperature changes mask the localized response. By means of the differential-thermistor probe, it is possible to eliminate the general temperature change and yet record localized thermal activity. This probe consists of 2 matched thermistor beads (VECO 41A14) vertically separated by 3mm. A small piece (3 mm) is broken off the four-hole alumina rod. One of the matched thermistor beads is placed at the tip of this 3 mm piece and the second bead is placed at the tip of the longer portion of the rod. After the wires from the thermistors are threaded through the holes, the two pieces are reattached by means of the Epoxylite varnish. Thus, a single probe is constructed which has 2 matched thermistors incorporated into the alumina rod and vertically separated by 3 mm (see Fig. 1C). The probe is placed in the brain with the lower bead in the area of interest while the upper head is placed just outside of this area. Both beads record generalized temperature changes but localized thermal responses are recorded primarily on the lower bead. By placing the 2 thermistors in adjacent arms of a Wheatstone bridge (see Fig. 5) the general temperature changes are cancelled and a recording of localized thermal activity is attained. Figure 4 is an example of recordings made with a differential-thermistor probe.

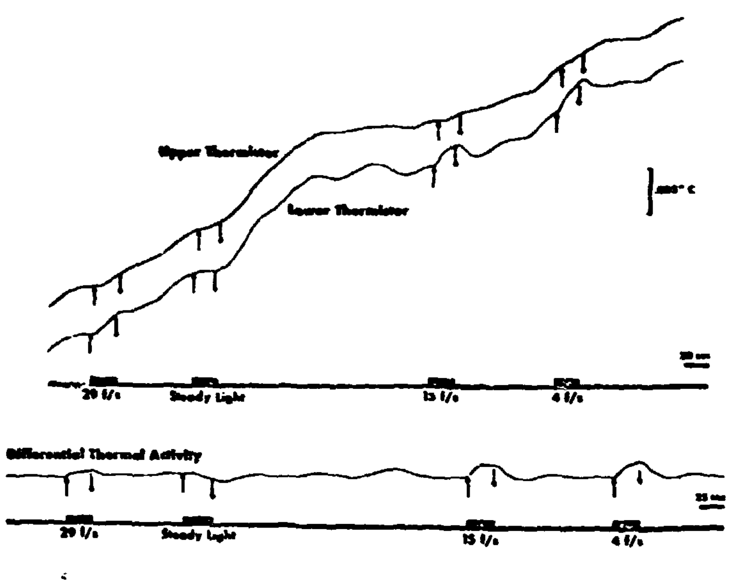
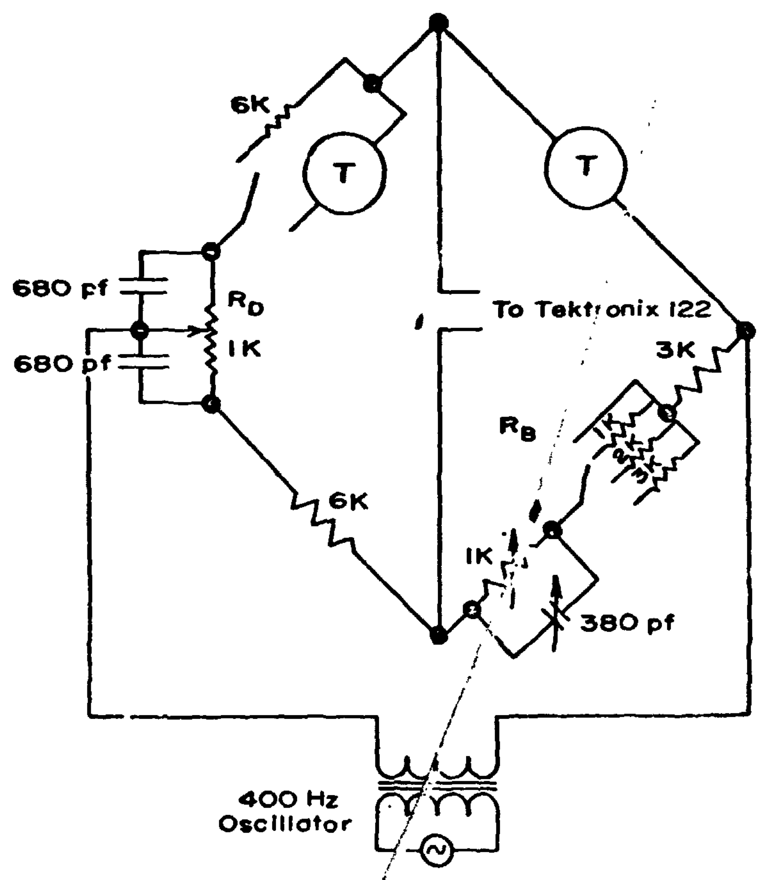


Figure 4. Results obtained with a differential-thermistor probe (3 mm thermistor separation). Top: thermal record obtained from the lateral geniculate nucleus (lower thermistor) and an area 3 mm above (upper thermistor). Bottom: resultant differential thermal activity. Arrows and time markers indicate periods when the eye was stimulated with flashing or steady light (2).

2.2 COMPENSATING RATIO BRIDGE

Although thermistors possess a relatively high coefficient of resistance and therefore considerable sensitivity to temperature change, they have the inherent disadvantage of displaying a non-linear relationship between resistance and temperature. One of the main drawbacks, then, is that the sensitivity of the thermistor changes over the temperature range. There is a need for a bridge circuit that has a linear relationship between the dial position at balance and the thermistor temperature. A relatively simple solution to this problem has been worked out by Doms (5). The bridge circuit depicted in Figure 5 is an adaptation of a temperature bridge suggested by him.

Doms noted that a ratio bridge is the first order approximation to the series expansion of ln $\underline{x}$. Therefore, the dial movement of the ratio resistance (R_D) necessary to obtain balance varies exponentially with temperature, the net effect is that the dial movement of R_D varies linearly with the temperature of the thermistor. (See 5) for a more comprehensive and detailed discussion).



R_D
R_B (variable) } 10 Turn Helipot 1KΩ Model A
Other resistors -.02 % wirewound

Figure 5. Circuit diagram for an a.c. compensating ratio bridge.

Inter-thermistor resistance variations at a single temperature which are due to manufacturing tolerances (± 25%) are compensated for by R_B. The resistance of a thermistor is obtained at one particular temperature. This value is chosen so that it is the midpoint of the temperature range used. For our particular application, 38.5°C is the temperature for which all the thermistors are calibrated. This particular temperature is the normal body temperature of the cat which is the animal used in our investigation. Only in rare circumstances does the temperature vary more than ± 2°C (3.6°F) from this value. Therefore, the temperature range encountered is very small. When other animals are to be used, their normal body temperature is chosen to be the midpoint. In the case of the human, this would be 37.0°C.

2.3 OPERATION OF THE BRIDGE

The a.c. compensating ratio bridge illustrated in Figure 5 is constructed so that at normal body temperature all arms have approximately equal resistances and therefore maximum bridge sensitivity is achieved. Furthermore, it has been adapted to be used with the 3 probes previously described. The thermistor of the thermistor-electrode probe (Figure IA) is inserted into the upper right hand arm of the bridge. The 6 kΩ resistance is used in the upper left hand arm. R_B is adjusted to the resistance of the thermistor at the mid-range temperature point. The bridge is now balanced by varying R_D and the temperature is read directly from this dial. For operation with the heated-thermistor probe (Figure IB) the same procedure is used. The only difference in using this probe is that the heater is connected to an external current supply which indirectly raises the temperature of the thermistor. For operation with the differential-thermistor probe (Figure IC), the 6 kΩ resistor in the upper left hand arm of the bridge is replaced with the second or reference thermistor and R_D is readjusted to achieve a balance. The absolute temperature cannot be read in this condition but localized temperature changes are obtained from the output of the bridge. If a temperature value is desired the bridge is operated in the single thermistor mode.

The various capacitors on the bridge circuit are to balance the reactive component due to stray capacitance and the capacitance of the thermistor cables. When a minimum is achieved by resistive balancing, the capacitor (380 pF) in the R_B arm is adjusted to further reduce this minimum.

2.4 BRAIN TEMPERATURE SYSTEM

One of the prime considerations in the design of a system to measure temperature changes in the brain was to make use of equipment generally available in a neurophysiology laboratory. An alternating current bridge was chosen because of the accessibility of high gain, low level a.c. amplifiers. As seen in Figure 6, the output of the bridge is fed into a Tektonix 122 Amplifier where the signal is amplified 1000 times. After narrowing the bandpass and demodulating the signal, the output is recorded on the D.C. channel of a Grass Polygraph Machine. Small temperature changes can be read in terms of pen displacements. In such a manner, several channels of temperature can be recorded on the same machine.

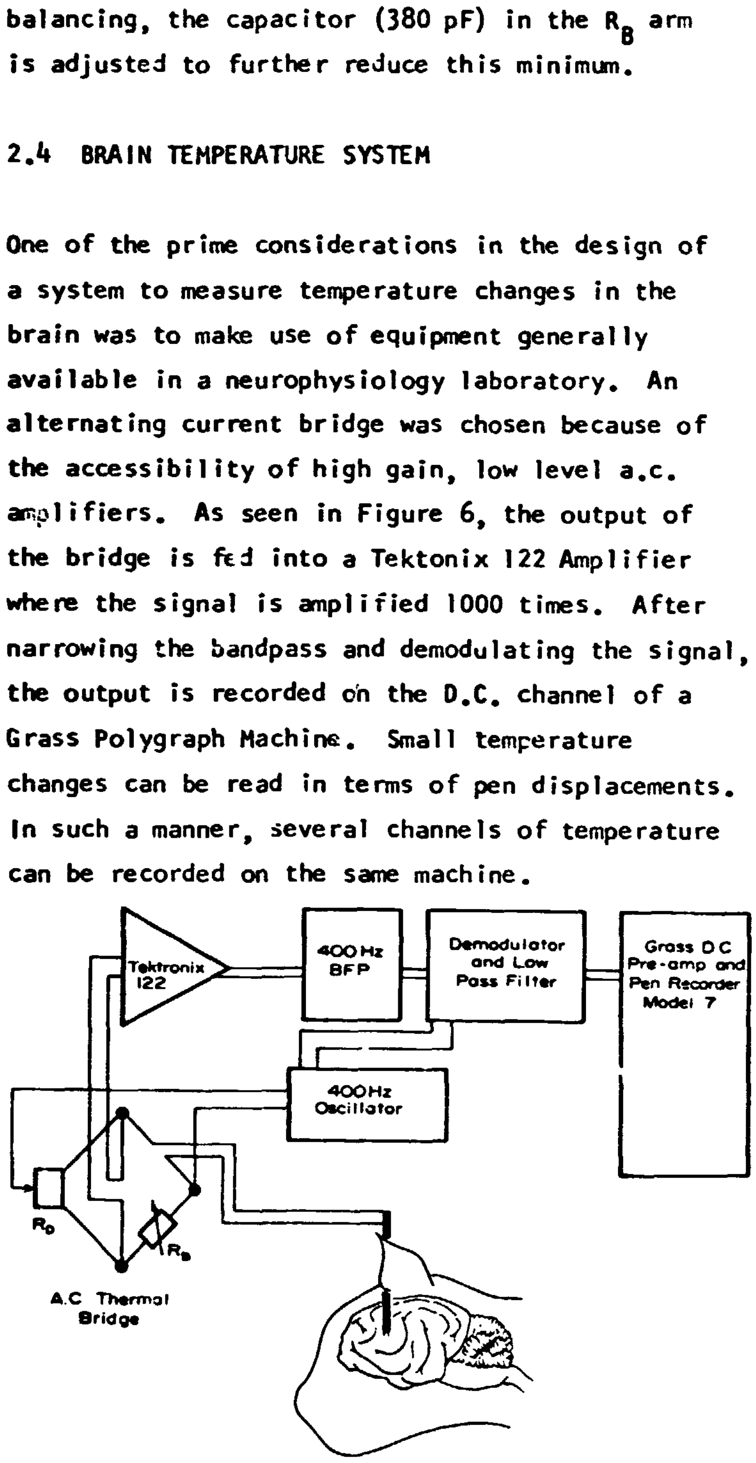


Figure 6. Various components of a thermal system used in the measuring of brain temperature.

2.5 CHARACTERISTICS OF THE SYSTEM

The system as described in Figures 5 and 6 allows us to read the temperature of thermistor beads with tolerances of ± 25% directly from the dial setting of the bridge. It is necessary to calibrate the thermistor for only one standard temperature. The bridge is calibrated in terms of dial settings (R_D) and d.c. output only once for use with one type of thermistor (VECO 41A14) that is used on the thermistor-electrode probe and the differential thermistor probe. It is calibrated a second time for use with the second type of thermistor (VECO 37A3) used in the heated-thermistor probe. The system with a thermistor implanted in the brain produces a self heating of not more than 0.01°C and possesses a time constant of 0.1 sec. Inasmuch as the temperature changes recorded in the brain are much slower than this, the time response of the system is adequate. Also, it has a measured noise equivalent of 0.00018°C and therefore can resolve very small temperature fluctuations. Over a ± 4°C range, the error introduced in reading the temperature as a linear function of the dial setting (R_D) is ± 1% for an individual thermistor. It has been noted that for a number of thermistors used, the linear assumption introduces a minimum error of ± 3% over this range. Since the range of temperature over which the animal normally varies is less than this, the system sufficiently linearizes the response of the thermistor to make it useful in measurements of brain and body temperature.

3. CONCLUSIONS

A system is presented by which various temperature measurements can be made in the brain. Three probes are used to detect various temperature phenomena. The thermistor-electrode probe is used to record general and localized temperature changes as well as the concomitant electrical activity of the nerve cells. The heated-thermistor probe aids in determining whether temperature changes are due wholly or partially to alterations in blood flow rates. The differential-thermistor probe is used to record localized thermal activity in the absence of temperature change that takes place throughout the brain.

An a.c. compensating ratio bridge linearizes the response of the thermistors to ± 3% over an 8°C range. It also allows thermistor beads with manufacturing tolerances of ± 25% to be used interchangeably in the system. Sufficient resolution is achieved by means of a bandpass filter and high gain/low noise preamplifier to make changes of .0002°C detectable.

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BIOGRAPHY

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